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Experiência de 6 Anos de Cirurgia Micrográfica de Mohs num Hospital Português

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RESUMO – Introdução: A cirurgia micrográfica de Mohs é um método cirúrgico de tratamento dos tumores cutâneos que consiste no controlo histológico das margens do tumor usando cortes horizontais em camadas finas congeladas a fresco. Esta técnica é uma indicação preferencial para tumores cutâneos da face (carcinoma basocelular e espinocelular, entre outros) associados a maior risco de recidiva, tumores recidivados, com margens clínicas indefinidas, quando existe envolvimento perivascular e perineural ou com subtipos histológicos agressivos. **Métodos:** Os autores realizaram um estudo retrospectivo de um período de 6 anos (de julho 2012 até junho 2018) num hospital Português – Hospital de Egas Moniz, para definir as características dos doentes submetidos a cirurgia micrográfica de Mohs e avaliar as vantagens desta técnica. Foram analisados os fatores: idade, género, proveniência, diagnóstico, localização do tumor, número de estádios da cirurgia micrográfica de Mohs, tipo de reconstrução do defeito cirúrgico, seguimento e recidiva. **Resultados:** Foram operados 835 tumores no total, 459 em doentes do sexo masculino e 376 em doentes do sexo feminino. A média de idades foi de 71 anos (intervalo entre 23- 95 anos). A maioria dos tumores submetidos a cirurgia micrográfica de Mohs foram carcinomas basocelulares (87%) localizados na pirâmide nasal (43%). Em 44% dos casos, houve necessidade de realizar mais de um estadiamento micrográfico. Metade dos encerramentos do defeito cirúrgico foram realizados por enxerto ou retalho cutâneo. Em doentes com seguimento igual ou superior a 3 anos, a taxa de recidiva foi de 4,9%. **Discussão:** O diagnóstico mais frequente foi o de carcinoma basocelular, o que reflete a importância da cirurgia micrográfica de Mohs, neste tipo de neoplasia cutânea, quer em lesões primárias como persistente/recorrentes. Salientamos que comparativamente a outras revisões europeias de cirurgia de Mohs, a taxa de recidiva dos tumores se encontra dentro dos parâmetros normais. Este dado é particularmente relevante, se considerarmos que o nosso serviço recebe doentes enviados de hospitais e dermatologistas de todo o país, especialmente selecionados quanto à agressividade tumoral ou já recidivados. O intervalo médio de recorrência para MMS foi de 27,9 meses, o que demonstra a necessidade de um seguimento a longo prazo destes doentes. **Conclusão:** A cirurgia micrográfica de Mohs permite menores taxas de recidiva comparativamente à excisão cirúrgica simples pelo que a sua prática deve ser encorajada em tumores devidamente selecionados. O controlo cirúrgico das margens em vez das “margens cegas” é uma mais-valia tanto na poupança de tecido sã como na garantia da excisão completa do tumor num mesmo tempo cirúrgico.

PALAVRAS-CHAVE – Cirurgia de Mohs; Neoplasias da Pele; Portugal.

6 Years' Experience of Mohs Micrographic Surgery in a Portuguese Hospital

ABSTRACT – Introduction: Mohs micrographic surgery (MMS) is a surgical method of treating skin tumors that consists of histological control of the tumor margins using horizontal slices in thin, freshly frozen layers. This technique is a preferred indication for cutaneous facial tumors (basal and squamous cell carcinoma, among others) associated with higher risk of recurrence, recurrent tumors, tumors with undefined clinical margins, when there is perivascular and perineural involvement or with aggressive histological subtypes. **Methods:** The authors carried out a retrospective study of a 6-year period (from July 2012 until June 2018) at a Portuguese hospital – Egas Moniz hospital, to define the characteristics of patients undergoing Mohs micrographic surgery and to evaluate the advantages of this technique. The following factors were analyzed: age, gender, provenience, diagnosis, tumor location, number of stages of MMS, type of reconstruction of the surgical defect, follow-up and recurrences. **Results:** A total of 835 tumors were excised, 459 in male patients and 376 in female patients. The mean age at surgery was 71 years old (range 23- 95 years). Most of the lesions submitted to MMS were basal cell carcinomas (87%) and the most common location was the nasal

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pyramid (43%). In 44% of the cases, it was necessary to perform more than one micrographic stage. Half of the surgical defect closures were performed by graft or skin flap. Considering patients with a follow up equal or superior to 3 years, the recurrence rate was 4.9%. **Discussion:** The most frequent diagnosis was basal cell carcinoma, reflecting the importance of MMS in this type of skin malignancy, in both primary and persistent/recurrent lesions. Compared to other European surgery reviews, our recurrence rate is within normal range. This fact is particularly relevant, if we consider that our institution receives patients sent from hospitals and dermatologists from all over the country, specially selected for tumor aggressiveness or previous relapse. More than half of these patients were referred from other centers and consisted of persistent/recurrent basal cell carcinomas. The follow-up at recurrence for MMS was 27.9 months, supporting that a long follow-up of these patients is necessary. **Conclusion:** MMS allows lower rates of recurrence compared to simple surgical excision, so its practice should be encouraged in selected tumors. The surgical control of the margins instead of the “blind margins” is an advantage in saving healthy tissue and allows the complete excision of the tumor in the same surgical time.

KEYWORDS – Mohs Surgery; Portugal; Skin Neoplasms / surgery.

INTRODUCTION

Skin cancer is the most common malignancy, with basal cell carcinoma (BCC) being the most common type, followed by squamous cell carcinoma (SCC). In the last decades, there has been a rise in the incidence of nonmelanoma skin cancers.¹

Mohs micrographic surgery (MMS) is a surgical technique that allows evaluation of the entire peripheral and deep margins of excised skin malignancies, leading to higher cure rates, compared to conventional excision.²

MMS also preserves the maximum normal adjacent tissue possible, resulting in smaller resection defects, and this can be especially important in aesthetic and functional areas, as in the face.^{1,2}

MMS represents an option for different types of skin malignancies, ranging from basal cell carcinoma, squamous cell carcinoma, atypical fibroxanthoma, dermatofibrosarcoma protuberans, Merkel cell carcinoma, microcystic adnexal carcinoma, sebaceous carcinoma, eccrine porocarcinoma, leiomyosarcoma, extramammary Paget's disease, aggressive digital papillary adenocarcinoma and even melanoma.² It can be used for the treatment of primary or recurrent/persistent tumors.³

This technique involves a series of steps that ensue in tumor excision, while allowing the repair of the surgical defect on the same day.² Despite being regarded as a laborious technique, different studies have shown a superior benefit/cost as compared to conventional excisions or radiotherapy.⁴

Candidates for this procedure include: large lesions (measuring >2 cm), aggressive histological subtypes of BCC and SCC, ill-defined margins, incompletely excised or recurrent lesions and high-risk anatomical locations (such as central face, eyebrows, eyelids, periorbital area, nose, lips, chin, mandible, preauricular and retroauricular areas, temple, ears, genitals, areola, nipples, hands and feet).⁵⁻⁷

There is a paucity of Portuguese centers performing MMS surgery, making our institution an unofficial referral center for patients from all over the country, with more aggressive, recurrent or high-risk tumors.

We present a retrospective study of all patients submitted to MMS surgery during a period of 6 years in a Portuguese Dermatology Department.

MATERIAL AND METHODS

Patients

The study was conducted at the Department of Dermatology at Egas Moniz hospital in Lisbon, Portugal. We retrospectively analyzed all patients who have undergone MMS between July 2012 and June 2018.

The indications for MMS were tumor site (especially central face), tumor size (especially >2 cm), poor clinical definition of tumor margins and recurrent lesions.

Most tumors were selected clinically, without a confirmatory cutaneous biopsy.

Surgical Procedure

The surgical procedure started with outlining the tumor margins with ink, before administering local anesthesia. After this, the tumor was removed or “debulked” with a scalpel or curette. Following this, tumors were excised at an angle of 45° and the specimen was divided into sizes appropriate for frozen sectioning and marked with colored dyes to enable mapping of the tumor. The tissue stains used were hematoxylin and eosin (H&E) and toluidine blue (if basal cell carcinoma was suspected). After that, the surgeon evaluated the margins microscopically. If the margins proved to be positive, another MMS stage was performed. If the margins were negative, the surgeon would proceed with the repair of the surgical defect.

Reconstruction of the surgical defect was performed on the same day of tumor excision, except for the cases left for secondary intention or referred to other surgical specialties (like Plastic surgery and Otorhinolaryngology). Every surgery was performed or supervised by a Mohs surgeon certified by the European Society for Micrographic Surgery.

Data Analysis

We evaluated factors such as: age, gender, provenience, diagnosis, tumor location, number of stages of MMS, type of reconstruction of the surgical defect, follow-up and recurrences.

In terms of tumor recurrence or persistence after surgery, we defined persistent tumors as tumors that were present despite treatment with topical chemotherapeutics, cryotherapy, electrodesiccation and curettage or simple excision in the previous 6 months. Tumors were defined as recurrent

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if a previous treatment had been performed more than 6 months before.

RESULTS

In total, during these 6 years, MMS was carried out on 835 patients, 459 (55%) males and 376 (45%) females with a median age at surgery of 71 years (range 23–95 years). Most patients (59%) were followed at the department of Dermatology of Egas Moniz hospital. The rest of the patients was referred from different institutions, either private or public hospitals (Fig. 1).

The most frequent diagnosis after histopathological evaluation was basal cell carcinoma accounting for 79% of the total of lesions ($n=728$ tumors), followed by squamous cell carcinoma (6.3%, $n=53$ tumors). The other excised lesions were actinic keratosis (1.8%, $n=15$), dermatofibrossarcoma protuberans (1.4%, $n=12$), atypical fibroxanthoma (0.2%, $n=2$), Merkel carcinoma (0.1%, $n=1$), verrucous carcinoma (0.1%, $n=1$), malignant melanoma (0.1%, $n=1$), porocarcinoma (0.1%, $n=1$) and keratoacanthoma (0.1%, $n=1$) (Table 1). In 2.4% of cases no lesion was found, despite the fact that some of these lesions had a prior biopsy confirming cutaneous malignancy.

The two most frequent diagnosis were basal cell carcinoma and squamous cell carcinoma, mainly primary (69.5% and 69.8%, corresponding respectively to 506 and 37 tumors). The remaining cases were recurrences (20.1% and 17%, corresponding respectively to 146 and 9 tumors) or persistence (8.2% and 1.9%, corresponding respectively to 60 and 6 tumors) after either conventional excision or MMS.

Table 1 - Histopathological diagnosis from tumors excised by MMS.

Excised lesions	Number of surgeries
Basal cell carcinoma	728
Squamous cell carcinoma	53
Absence of tumor*	20
Actinic keratosis	15
Dermatofibrossarcoma protuberans	12
Atypical fibroxanthoma	2
Merkel carcinoma	1
Verrucous carcinoma	1
Malignant melanoma	1
Porocarcinoma	1
Keratoacanthoma	1
Total	835

* Some cases with a biopsy proven basal cell carcinoma, had histopathology without malignancy after MMS.

The most common tumor location was the nose (43%, $n=113$). Lesions located on the scalp, trunk, abdomen, limbs and lumbar areas were excised by MMS given the

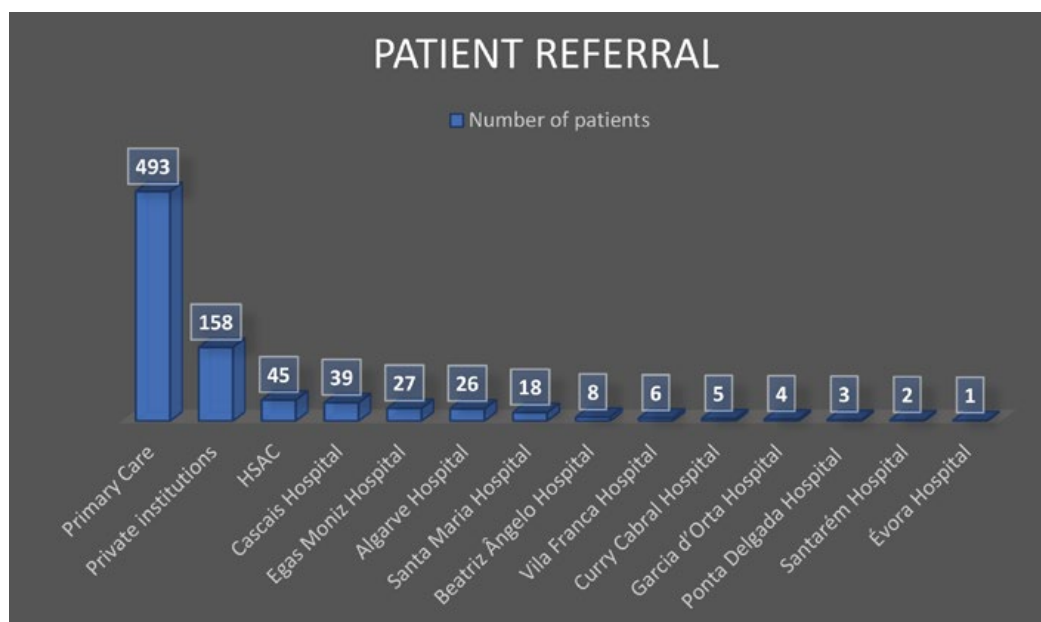


Figure 1 - Patient referral. Most patients were followed at dermatology consultation of Egas Moniz hospital after referral from primary care. Patients that came directly from Egas Moniz Hospital, were referred from other surgical specialties, such as, Plastic surgery. HSAC – Hospital Santo António dos Capuchos.

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extensive dimensions or poorly defined margins. A detailed location is present on Table 2.

The number of stages of MMS required to excise the entire lesion ranged from one to seven. Most frequently, only one stage was necessary (56%, n=468) for removing the complete lesion. Just one case needed seven stages and it ended up being negative, confirming the total removal of the malignancy (Fig. 2).

The resection was completed in 98.2% of the lesions

Table 2 - Location of the excised tumors by anatomical area.

Tumor location	Number of tumors
Nose – dorsum	113
Nose – wings	107
Nose – nasolacrimal sulcus	58
Nose - tip	56
Zygomatic region	51
Scalp	48
Forehead	43
Temporal region	38
Retroauricular region	29
Eye – inferior eyelid	26
Eye – inner cantus	25
Preauricular region	24
Ear - lobule	23
Ear – helix	21
Nasogenian sulcus	20
Supraciliar region	20
Mental region	16
Glabella	15
Cheek	14
Trunk	9
Eye – outer cantus	6
Eye – superior eyelid	6
Ear – concha	6
Scapular region	5
Abdomen	4
Limbs	3
Nose - columella	3
Ear - tragus	2
Neck	2
Inferior lip	2
Lumbar region	1
Total	835

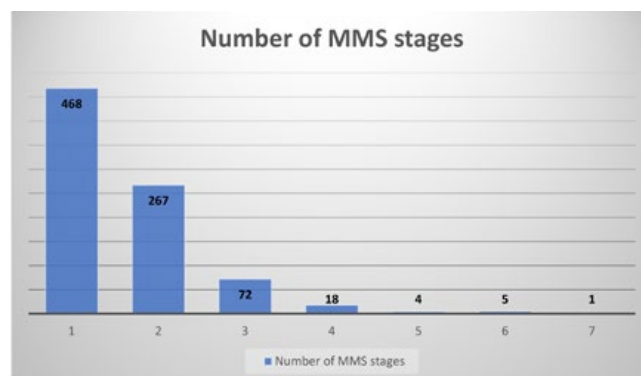


Figure 2 - Number of MMS stages performed in each patient.

(n=820). In 15 cases, it was not possible to remove the whole lesion, because of an extensive surgical defect, deep invasion of the tumor or patient refusal to proceed with the surgery.

For repairing the surgical defect, linear closure was the principal option (41%, n=342), but in about half the cases, it was necessary to perform a skin graft or skin flap, reflecting the complexity of the surgical defects created after tumor excision (Fig. 3). Skin flaps that were performed were: transposition flap (13.4%, N=112), advancement flap (8.7%, n=73), rotation flap (4.9%, n=41), A-T flap (2.8%, n=23) and island flap – V-Y myocutaneous (2.3%, n=19). The remaining cases consisted of closure by other surgical specialties (4.8%, 37 were performed by Plastic Surgery and one case by Otorhinolaryngology) or closure by secondary intention (5%, n=43).

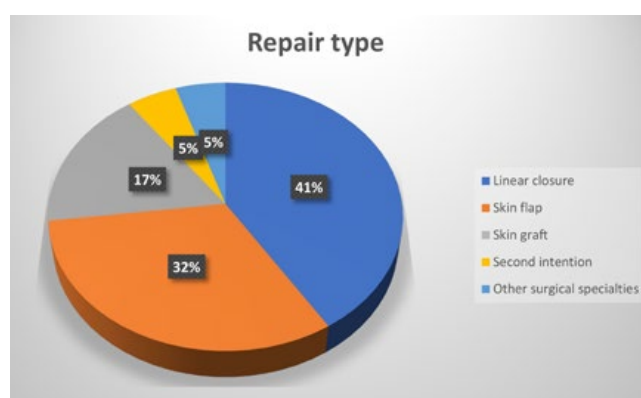


Figure 3 - Type of repair of the surgical defect after MMS.

The maximum follow-up registered was 77 months. Two hundred and thirty three patients (28%) had a follow up inferior to 3 months, 381 (46%) had a follow-up between 3 months and 3 years and 221 (26%) patients were followed for more than 3 years. Considering patients with a follow-up equal or superior to 3 years, the recurrence rate was 4.9%

(11 patients) and they were all basal cell carcinomas. Their histological subtypes were infiltrative (5 patients), morpheaform (3 patients), ulcerative (2 patients) and micronodular (1 patient). Of these, 54.5% were referred from other hospitals, had more than 2 stages of MMS performed and 54.5% needed closure of the surgical defect by a flat or a graft. 54.5% were female patients and the median follow-up at recurrence was 27.9 months (Table 3).

DISCUSSION

Our data are in accordance with other studies, concerning the median patient age at surgery.^{1,6} A considerable amount (41%) of patients were referred from other Portuguese centers, although our department is not an official reference center for MMS.

The most frequent diagnosis was basal cell carcinoma, reflecting the higher prevalence of this skin malignancy, but also the importance of MMS, in the treatment of both primary and persistent/recurrent lesions, as reported in different series where MMS offers 5-year cure rates of 99%, for primary BCC and 94.4% for recurrent BCC, which are superior if we compare with conventional excision (90 % for primary BCC and 80% for recurrent BCC).²

As stated, MMS has clear advantages when dealing with lesions where "saving skin" is fundamental.^{5,7} Therefore, lesions on the facial area, mainly the nasal pyramid, were the most frequently excised. This offers greater aesthetic and functional results with smaller surgical defects, when comparing with conventional excision.^{1,2}

As for the number of stages of MMS required to excise the entire lesions, in 44% more than 2 stages were necessary, reflecting the higher surgical difficulty of the tumors.

Only considering patients with a follow-up superior to three years, a recurrence rate of 4.9% was recorded, which falls within the interval reported by European databases

(1.7-6.7%).^{8,9} Reasons for explaining recurrence after MMS are failure to excise more tissue when a dense inflammatory infiltrate is present, presence of residual tumor at the margins, missing epidermis or dermis, multifocal tumor and wrong inking of the lesion.¹⁰ In our case, recurrence results may also be due to a higher complexity of the tumors (larger, more infiltrative and more aggressive) as more than half of these patients with recurrent disease were complex cases, referred from other centers, mostly persistent/recurrent basal cell carcinomas that needed closure by skin flap or skin graft.

We evaluated only patients with a follow-up > 3 years to avoid underestimation of recurrence in case of short follow-up, as most recurrences are reported after 5 years of treatment.¹¹ This is in agreement with our late recurrence after MMS (27.9 months), supporting that a long follow-up of these patients is necessary.

Limitations

As a retrospective study there are several limitations in our study.

Some patients had a short follow-up as for those referred from other hospitals they were referred back to their original hospital after the evaluation at 2-3 months with consequent loss of follow-up, and in other cases several patients missed their appointments.

Unfortunately, not all patients had a cutaneous skin biopsy before MMS, which led to unnecessary surgery in cases of actinic keratosis (1.8%). Despite this, the overall diagnosis accuracy was high, given that all the other excised tumors had an indication to be removed.

Also, some indications to perform MMS, like presence of neurological symptoms and state of immunosuppression were not represented in our review, as we only considered tumor size or anatomical area of high-risk.

Table 3 - Characteristics of the recurrences after MMS.

Age	Gender*	Referral	Diagnosis	MMS stages	Reconstruction	Follow-up at recurrence ^a
74	F	Primary care	Primary BCC	1	Linear closure	20
69	F	Cascais hospital	Persistent BCC	1	A-T flap	22
75	M	Primary care	Recurrent BCC	3	Graft	34
34	M	Egas Moniz hospital	Recurrent BCC	1	Graft	32
59	F	Egas Moniz hospital	Primary BCC	1	Graft	39
69	M	Private institution	Primary BCC	2	Linear closure	43
85	M	Cascais hospital	Recurrent BCC	3	Graft	12
62	M	Private institution	Recurrent BCC	7	Graft	20
68	F	Private institution	Recurrent BCC	2	Graft	15
79	F	Primary care	Primary BCC	1	Linear closure	44
75	F	Primary care	Primary BCC	2	Secondary intention	26

* F refers to female and M to Male. ^a Follow-up is expressed in months after the initial surgery

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CONCLUSION

Mohs micrographic surgery allows lower rates of recurrence compared to simple surgical excision, so its practice should be encouraged in selected tumors. The surgical control of the margins instead of the "blind margins" is an advantage in saving healthy tissue, as it allows the complete excision of the tumor in the great majority of the cases, resulting in lower recurrences and a higher patient satisfaction.

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Proteção de pessoas e animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pelos responsáveis da Comissão de Investigação Clínica e Ética e de acordo com a Declaração de Helsinquia da Associação Médica Mundial.

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